Solid-State Assisted Synthesis of Oligobenzoates

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1 Materials and Chemicals

All chemicals were purchased from commercial suppliers *Alfa Aesar*, *Merck*, *Acros*, *Sigma Aldrich* and *Nova Biochem* and were used without further purification. The solvents were distilled prior to use.

Column chromatography: Glass-columns were individually packed with Silica gel (pore size: 60 Å, 70.230 mesh, 63-200 µm, *Sigma Aldrich*).

TLC-sheets: ALUGRAM[®] Xtra SIL G/UV₂₅₄, Silica gel 60 (*Macherey-Nagel*).

2 Technical Equipment

Solid-Phase Synthesis: Heidolph *Synthesis 1* Parallel Synthesizer.

This equipment - consisting of 16 reaction vessels of 42 ml each - allows the addition of samples, splitting off or cleaving from the resin, filtration of by-products and purification of the product. The reaction vessels are made of chemically resistant polytetrafluorethylene (PTFE) and perfluoroalkoxy alkanes (PFA) material. The resin will not stick to the inner walls of the vessel and provides clear visibility of the sample. Shaking the reaction prevents the attrition of the fine grained Wang resin by a magnetic stir bar. The vessels are easily and quickly refilled via a needle through the septa. The bottom part of the reaction vessel consists of the filter (pore size 25 µm), valve and tube connector for vacuum filtration. The fractions are collected via vacuum filtration in a waste cube of glass. After the synthesis process, the product will be recovered by vacuum and collected in test tubes.^[1]

In this publication we exclusively work with Wang resin, thus we use DCM as solvent for the swelling, washing and coupling reactions.

Note! The parallel synthesizer is especially convenient for the present synthesis. However, the synthesis may be performed also with conventional glassware on a laboratory shaker.

NMR spectroscopy: Bruker-Daltonics *Avance-400* spectrometer operating at 400 MHz (^1H) or 100 MHz (^{13}C) or Bruker-Daltonics *Ascend-600* operating at 600 MHz (^1H) or 151 MHz (^{13}C). Chemical shifts are indicated in ppm in relation to the particular internal standard (^1H NMR: 7.26 ppm for CDCl_3 , 2.50 ppm for DMSO-d_6 ; ^{13}C NMR: 77.16 ppm for CDCl_3 and 39.52 ppm for DMSO-d_6). Signal multiplicities are denoted as s (singlet), d (doublet), t (triplet) and m (multiplet). Processing of the raw data was performed with the program Topspin 3.0.^[2]

Mass spectroscopy (MALDI): Bruker-Daltonics *autflex II*.

Elemental Analysis: Elementar CHNS 932 analyzer (Institute of Inorganic Chemistry)

Preparative recycling gel permeation chromatography: Liquid chromatograph *LC-20A* (Shimadzu). The column set (PSS *SDV* 50 Å, 20·600 mm; PSS *SDV* 500 Å, 20·600 mm) was eluted with HPLC-grade CHCl_3 at a flow rate of $4.0 \text{ ml} \cdot \text{min}^{-1}$.

Polarised optical microscopy: Melting and clearing temperatures were determined with a Nikon *Eclipse LV100Pol* optical polarizing microscope equipped with a Linkam *LTS420* heating stage and a Linkam *T95-HS* system controller.

3 Synthetic Procedures and Analytical Data

Graphical overview of the solid-phase synthesis

Abbreviations: DCM: dichloromethane, DMF: dimethylformamide, DPTS: dimethylpyridinium toluylsulfonate, DCC: dicyclohexylcarbodiimid, Et₂O: diethylether, DIC: diisopropylcarbodiimid, TBAF: tetrabutylammonium fluoride, TFA: trifluoroacetic acid.

General procedure for the solid-phase synthesis with Wang resin of C(1-3)_pⁿ

Preparation: 1.0 g Wang resin (1.10 mmol/g) is swollen in 15 ml DCM for 2 h at room temperature and subsequently washed with 2 x 15 ml DCM.

Step 1: a) Coupling of the repeating unit: 2.0 eq (2.20 mmol, 0.55 g) silyl-protected *p*-hydroxybenzoic acid, 0.8 eq (0.88 mmol, 0.26 g) DPTS and 15 ml DCM are mixed and – after 5 minutes – 2.0 eq (2.20 mmol, 0.35 ml) DIC are added. The mixture is shaken for 12 h and the solution is subsequently removed by filtration.

b) Washing procedure: The resin is washed with 15 ml DCM, 15 ml methanol and 15 ml DCM.

Step 2: a) Cleavage of the silyl group: The vessel with the resin is charged with 3.0 eq (3.30 mmol, 0.95 g) TBAF, 3.5 eq (3.85 mmol, 0.20 ml) acetic acid and 15 ml THF and shaken for 2 h at room temperature before the solvent is removed by filtration.

b) Washing procedure (see step 1 b)

Step 3: a) Coupling of the peripheral unit: 2.0 eq (2.20 mmol) of the individual head group, 0.8 eq (0.88 mmol, 0.26 g) DPTS and 15 ml DCM : DMF (1 : 2) are mixed and – after 5 minutes – 2.0 eq (2.20 mmol, 0.35 ml) DIC are added. The mixture is shaken for 12 h and the solvent is subsequently removed by filtration.

b) Washing procedure (see step 1 b)

Step 4: Cleavage from the resin: The resin is shaken for 2 h with 15 ml cleavage solution (90 % TFA, 7.5 % triethylsilane, 2.5 % water). After filtration the resin is washed twice with 15 ml DCM. The solvent of the combined liquids is removed in vacuum.

Isolation and purification: adopted and optimized for each product.

General procedure for the conventional synthesis in solution of C(1-3)_pⁿ

- Step 1: To a solution of 1.0 eq of the individual head group and 2.0 eq of benzyl-4-hydroxybenzoate in DCM a solution of 0.8 eq DPTS and 2.0 eq DCC in DCM is added and the mixture is stirred at room temperature for 17 h. The solvent is removed in vacuum and the resulting crude product is purified by column chromatography.
- Step 2: The protected arm is dissolved in THF and a catalytic amount of Pd/C is added. The mixture is stirred under H₂-atmosphere. The reaction progress is controlled by TLC. After the conversion was completed the catalyst is filtered through celite 545 and the solvent is removed in vacuum to obtain the deprotected arm product as a colorless solid or an oil depending on the nature of the peripheral chains.
- Step 3: To a solution of 1.0 eq of the arm (step 2) and 2.0 eq of benzyl-4-hydroxybenzoate in DCM a solution of 0.8 eq DPTS and 2.0 eq DCC in DCM is added and the mixture is stirred at room temperature for 12 h. The solvent is removed in vacuum and the resulting crude, elongated and still protected arm is purified by column chromatography.
- Step 4: The benzyl protected arm (step 3) is dissolved in THF and a catalytic amount of Pd/C is added. The mixture is stirred under H₂-atmosphere until completion (TLC-control). The catalyst is filtered through celite 545 and the solvent is removed in vacuum to obtain the deprotected product.

4-[3,4,5-tris(dodecyloxy)benzoyloxy]benzoic acid (**1₃¹**)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 - 4 were performed as described in the general procedure. In step 4 1.2 eq (1.32 mmol, 890 mg) of the head group 3,4,5-tris(dodecyloxy)benzoic acid are added. After cleavage from the resin, the crystallization from acetone afforded 580 mg (0.73 mmol, 66 %) of a colorless solid (m.p. 91 °C, lit. [3] m.p. 92 °C).

Synthesis in solution:

1₃¹ was synthesized in solution (73 %) according to the literature procedure [3].

Analytical data from the solid-phase synthesis:

¹H NMR (CDCl₃, 400 MHz): δ [ppm] = 0.86-0.91 (m, 9H, CH₃), 1.22-1.40 (m, 48H, CH₂), 1.45-1.52 (m, 6H, CH₂) 1.73-1.86 (m, 6H, CH₂), 4.03-4.08 (m, 6H, OCH₂), 7.30-7.34 (AA'BB', 2H, CH, H-4/4'), 7.40 (s, 2H, CH, H-8/8'), 8.17-8.20 (AA'BB', 2H, CH, H-3/3'). The analytical data agrees with the data of reference [3].

4-{4'-[4-(dodecyloxy)benzoyloxy]benzoyloxy}benzoic acid (**1₁²**)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 and 2 of the general procedure were performed twice followed by steps 3 and 4. In step 4 2.0 eq (2.20 mmol, 670 mg) of the head group 4-dodecyloxybenzoic acid are added. After cleavage from the resin,

the crystallization from acetone afforded 400 mg (0.73 mmol, 67 %) of a colorless solid (m.p. 185 °C, clearing > 300 °C under decomposition; lit. [4] m.p. 171-173 °C).

Synthesis in solution:

1₁² was synthesized in solution (52 %) according to the literature procedure [4].

Analytical data from the solid-phase synthesis:

¹H NMR (CDCl₃, 400 MHz): δ [ppm] = 0.87-0.90 (m, 3H, CH₃), 1.22-1.38 (m, 16H, CH₂), 1.44-1.52 (m, 2H, CH₂), 1.79-1.86 (m, 2H, CH₂), 4.06 (t, 2H, OCH₂), 6.97-7.01 (AA'BB', 2H, CH, H-14/14'), 7.34-7.37 (AA'BB', 2H, CH, H-9/9'), 7.37-7.41 (AA'BB', 2H, CH, H-4/4'), 8.13-8.17 (AA'BB', 2H, CH, H-13/13'), 8.18-8.22 (AA'BB', 2H, CH, H-8/8'), 8.27-8.30 (AA'BB', 2H, CH, H-3/3'). The analytical data agrees with the data of reference [4].

4-{4'-[3,4-di(dodecyloxy)benzoyloxy]benzoyloxy}benzoic acid (1₂²)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 and 2 of the general procedure were performed twice followed by steps 3 and 4. In step 4 2.0 eq (2.20 mmol, 1.08 g) of the head group 3,4-di(dodecyloxy)benzoic acid is added. After cleavage from the resin, the crystallization from acetone afforded 280 mg (0.38 mmol, 35 %) of a colorless solid (m.p. 155 °C, clearing temperature T_{cl} = 206 °C, m.p. (preparation by conventional solution method; this work) 155 °C, T_{cl} = 209 °C).

Synthesis in solution:

Step 1: 1.73 g (3.52 mmol) 3,4-di(dodecyloxy)benzoic acid and 803 mg (3.52 mmol) benzyl-4-hydroxybenzoat in 70 ml DCM, 207 mg (704 μmol) DPTS and 872 mg (4.22 mmol) DCC are added, reaction time 24 h. The solvent is removed in vacuum and the resulting crude product is dissolved in CHCl₃ and precipitated in EtOH; Step 2: reaction time 27 h;

Step 3: 2.00 g (3.28 mmol) 4-((3,4-di(dodecyloxy)benzoyl)oxy)benzoic and 747 mg (3.28 mmol) benzyl-4-hydroxybenzoat in 50 ml DCM, 386 mg (1.31 mmol) DPTS and 810 mg (3.94 mmol) DCC are added; reaction time 26 h; Step 4: reaction time 24 h; Yield: 2.16 g (2.96 mmol, 83 %) of a colorless solid.

Analytical data from the solid-phase synthesis:

¹H NMR (CDCl₃, 400 MHz): δ [ppm] = 0.86-0.90 (m, 6H, CH₃), 1.20-1.41 (m, 32H, CH₂), 1.46-1.53 (m, 4H, CH₂), 1.82-1.91 (m, 4H, CH₂), 4.06-4.11 (m, 4H, OCH₂), 6.95 (d, 1H, CH, ³J_{16,17} = 8.53 Hz, H-16), 7.34-7.41 (AA'BB', 4H, CH, H-4/4', H-9/9'), 7.67 (d, 1H, CH, ⁴J_{15,17} = 2.21 Hz, H-13), 7.84 (dd, 1H, CH, ³J_{17,16} = 8.46 Hz, ⁴J_{17,13} = 2.08 Hz, H-17), 8.20-8.24 (AA'BB', 2H, CH, H-8/8'), 8.28-8.31 (AA'BB', 2H, CH, H-3/3'); **¹³C NMR** (CDCl₃, 100 MHz): δ [ppm] = 14.28 (CH₃), 26.12, 26.16 (CH₂, C-20), 22.85, 29.17, 29.30, 29.52, 29.56, 29.77, 29.78, 29.82, 29.85, 32.08 (CH₂), 69.24, 69.52 (OCH₂), 112.04 (CH, C-16), 114.69 (CH, C-13), 120.98 (Cq, C-15), 122.09, 122.42 (CH, C-4/4', C-9/9'), 124.75 (CH, C-17), 126.49 (Cq, C-10), 126.97 (Cq, C-5), 132.07, 132.11 (CH, C-3/3', C-8/8'), 148.87 (Cq, C-14), 154.30 (Cq, C-12), 155.38 (Cq, C-7), 155.82 (Cq, C-2), 164.04 (C=O, C-1), 164.60 (C=O, C-11), 170.41 (C=O, C-6); **HRMS (ESI)**: m/z (%): calcd: 731.4523 ([M+H]⁺, 100), found: 731.4519 ([M+H]⁺, 100); **Elemental analysis** (%) for C₄₅H₆₂O₈: calcd: C 73.94, H 8.55, found: C 73.73, H 8.54.

4-{4'-[3,4,5-tris(dodecyloxy)benzoyloxy]benzoyloxy}benzoic acid (1₃²)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 and 2 of the general procedure were performed twice followed by steps 3 and 4. In step 4 2.0 eq (2.20 mmol, 1.48 g) of the head group 3,4,5-tris(dodecyloxy)benzoic acid is added. After cleavage from the resin,

the crystallization from acetone afforded 480 mg (0.52 mmol, 48 %) of a colorless solid (m.p. 81 °C, clearing temperature T_{cl} = 111 °C, lit. [5] m.p. 87 °C, T_{cl} = 114 °C).

Synthesis in solution:

1₃² was synthesized in solution (61 %) according to the literature procedures [3][5].

Analytical data from the solid-phase synthesis:

¹H NMR (CDCl₃, 400MHz): δ [ppm] = 0.86-0.90 (m, 9H, CH₃), 1.22-1.38 (m, CH₂, 48H), 1.45-1.53 (m, 6H, CH₂), 1.73-1.87 (m, 6H, CH₂), 4.04-4.09 (m, 6H, OCH₂), 7.34-7.39 (AA'BB', 4H, CH, H-4/4', H-9/9'), 7.41 (s, 2H, CH, H-13/13'), 8.19-8.23 (AA'BB', 2H, CH, H-8/8'), 8.27-8.31 (m, 2H, CH, AA'BB', H-3/3'). The analytical data agrees with the data of reference [5].

4-[3,4-di(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoyloxy)]benzoic acid (2₂¹)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 – 4 are performed according to the general procedure. In step 4 1.2 eq (1.32 mmol, 626 mg) of the head group 3,4-di(2-(2-(2-ethoxyethoxy)-ethoxy)ethoxy)benzoic acid is added. After cleavage from the resin, the crystallization from acetone afforded 600 mg (1.01 mmol, 92 %) of a colorless waxy solid (m.p. 84 °C, m.p. (conventional synthesis, this work) 85 °C).

Synthesis in solution:

Step 1: 4.00 g (8.43 mmol) 3,4-di(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoic acid and 3.85 g (16.9 mmol) benzyl-4-hydroxybenzoat in 40 ml DCM, 1.98 g (6.73 mmol) DPTS and 3.47 g (16.8 mmol) DCC in 10 ml DCM; Step 2: reaction time 6 d; Yield: 3.27 g (5.50 mmol, 66 %) of a colorless waxy solid.

Analytical data from the solid phase synthesis:

¹H NMR (CDCl₃, 400 MHz): δ [ppm] = 1.18 - 1.23 (m, 6H, CH₃), 3.49 - 3.56 (m, 4H, OCH₂, H-19), 3.57 - 3.78 (m, 16H, OCH₂), 3.89 - 3.93 (m, 4H, OCH₂, H-14), 4.22 - 4.27 (m, 4H, OCH₂, H-13), 6.98 - 7.01 (m, 1H, CH, ³J_{11,12} = 8.64 Hz, H-11), 7.29 -

7.33 (AA'BB', 2H, CH, H-4/4'), 7.69 (s, 1H, CH, $^4J_{8,12} = 2.08$ Hz, H-8), 7.82 - 7.85 (m, 1H, CH, $^3J_{12,11} = 8.50$ Hz, $^4J_{12,8} = 2.06$ Hz, H-12), 8.15 - 8.18 (AA'BB', 2H, CH, H-3/3'); **¹³C NMR** (CDCl₃, 100 MHz): δ [ppm] = 15.28 (CH₃), 66.78, 66.80 (OCH₂, C-19), 68.79 (OCH₂, C-13), 69.13 (OCH₂, C-14), 69.64, 69.78, 69.95, 70.83 (OCH₂, C-19), 112.9 (CH, C-11), 115.6 (CH, C-8), 121.7 (Cq, C-10), 122.1 (CH, C-4/4'), 125.1 (CH, C-12), 126.9 (Cq, C-5), 131.9 (CH, C-3/3'), 148.7 (Cq, C-9), 154.0 (Cq, C-7), 155.5 (Cq, C-2), 164.4 (C=O, C-6), 170.2 (C=O, C-1). **HRMS (ESI)**: m/z (%): calcd: 612.3020 ([M+NH₄]⁺, 100), found: 612.3016 ([M+NH₄]⁺, 100). **Elemental analysis** (%) for C₃₀H₄₂O₁₂: calcd: C 60.59, H 7.12, found: C 59.33, H 6.91.

4-[3,4,5-tris(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoyloxy)]benzoic acid (2₃¹)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 – 4 are performed according to the general procedure. In step 4 1.2 eq (1.32 mmol, 859 mg) of the head group 3,4,5-tris(2-(2-(2-ethoxy-ethoxy)ethoxy)ethoxy)benzoic acid are added. After cleavage from the resin, the crystallization from acetone afforded 780 mg (1.01 mmol, 92 %) of a colorless oil.

Synthesis in solution:

Step 1: 4.02 g (6.15 mmol) 3,4,5-tris(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoic acid and 2.80 g (12.3 mmol) benzyl-4-hydroxybenzoat in 40 ml DCM, 1.45 g (4.93 mmol) DPTS and 2.54 g (12.3 mmol) DCC in 10 ml DCM; Step 2: reaction time 4 d; Yield: 1.96 g (2.54 mmol, 43 %) of a colorless oil.

Analytical data from the solid phase synthesis:

¹H NMR (CDCl₃, 400 MHz): δ [ppm] = 1.17 - 1.22 (m, 9H, CH₃), 3.49 - 3.55 (m, 6H, OCH₂), 3.56 - 3.77 (m, 24H, OCH₂), 3.81 - 3.83 (m, 2H, OCH₂, H-12_{para}), 3.87 - 3.89 (m, 4H, OCH₂, H-12_{meta}), 4.21 - 4.24 (m, 4H, OCH₂, H-11_{meta}), 4.26 - 4.29 (m, 2H, OCH₂, H-11_{para}), 7.44 (s, 2H, CH, H-8/8'), 8.14 - 8.18 (AA'BB', 4H, CH, H-3/3',

H-4/4); ^{13}C NMR (CDCl_3 , 100 MHz): δ [ppm] = 15.24 (CH_3), 66.74 (OCH_2 , C-17), 69.14 (OCH_2 , C-11_{meta}), 69.74, 69.90, 69.92, 70.68, 70.71, 70.78, 70.81, 70.95 (OCH_2), 72.65 (OCH_2 , C-11_{para}), 109.9 (CH , C-8/8'), 121.9 (CH , C-4/4'), 123.7 (Cq , C-7), 127.4 (Cq , C-5), 131.9 (CH , C-3/3'), 143.7 (Cq , C-10), 152.6 (Cq , C-9/9'), 155.2 (Cq , C-2), 164.2 (C=O , C-6), 169.9 (C=O , C-1); **HRMS (ESI)**: m/z (%): calcd: 788.4069 ($[\text{M}+\text{NH}_4]^+$, 100), found: 788.4060 ($[\text{M}+\text{NH}_4]^+$, 100). **Elemental analysis** (%) for $\text{C}_{38}\text{H}_{58}\text{O}_{16}$: calcd: C 59.21, H 7.58, found: C 59.39, H 7.73.

4-{4'-[3,4-bis(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoyloxy)]benzoyloxy}-benzoic acid (2_2^2)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 and 2 of the general procedure were performed twice followed by steps 3 and 4. In step 4 1.2 eq (1.32 mmol, 626 mg) of the head group 3,4-di(2-(2-(2-ethoxyethoxy)ethoxy)ethoxy)benzoic acid are added. After cleavage from the resin, the crystallization from methanol afforded 700 mg (0.98 mmol, 89 %) of a colorless waxy solid (m.p. 103 °C).

Synthesis in solution:

Step 1 and 2: see synthesis of 2_2^1 ; Step 3: 1.46 g (2.52 mmol) 4-[3,4-di(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoyloxy)]benzoic acid and 1.15 g (5.04 mmol) benzyl-4-hydroxybenzoat in 20 ml DCM, 600 mg (2.02 mmol) DPTS and 1.04 g (5.04 mmol) DCC in 5.0 ml DCM; Yield: 145 mg (203 μmol , 25 %) colorless waxy solid.

Analytical data from the solid phase synthesis:

^1H NMR (CDCl_3 , 400 MHz): δ [ppm] = 1.19 - 1.23 (m, 6H, CH_3), 3.53 - 3.59 (m, 4H, OCH_2 , H-24), 3.60 - 3.79 (m, 16H, OCH_2), 3.91 - 3.95 (m, 4H, OCH_2 , H-19), 4.24 - 4.28 (m, 4H, OCH_2 , H-18), 6.98 - 7.00 (d, 1H, CH, $^3J_{16,17} = 8.60$ Hz, H-16), 7.35 - 7.40 (AA'BB', 4H, CH, H-4/4', H-9/9'), 7.70 (s, 1H, CH, $^4J_{17,13} = 2.00$ Hz, H-13),

7.84 - 7.86 (d, 1H, CH, $^3J_{17,16} = 8.44$ Hz, $^4J_{17,13} = 2.00$ Hz, H-17), 8.20 - .27 (AA'BB', 4H, CH, H-3/3', H-8/8'); ^{13}C NMR (CDCl_3 , 100 MHz): δ [ppm] = 15.30 (CH_3), 66.75 (OCH_2 , C-24), 68.93 (OCH_2 , C-18), 69.65 (OCH_2 , C-19), 69.91 - 71.00 (OCH_2), 112.8 (CH, C-16), 115.6 (CH, C-13), 121.6 (Cq, C-15), 122.0 (CH, C-9/9'), 122.2 (CH, C-4/4'), 125.1 (CH, C-17), 126.5 (Cq, C-10), 126.8 (Cq, C-5), 132.0 (CH, C-8/8'), 132.1 (CH, C-3/3'), 148.6 (Cq, C-14), 154.1 (Cq, C-12), 155.3 (Cq, C-7), 155.6 (Cq, C-2), 164.0 (C=O, C-1), 164.1 (C=O, C-11), 168.8 (C=O, C-6). **HRMS (ESI)**: m/z (%): calcd: 737.2785 ($[\text{M}+\text{Na}]^+$, 100), found: 737.2778 ($[\text{M}+\text{Na}]^+$, 100). **Elemental analysis** (%) for $\text{C}_{37}\text{H}_{46}\text{O}_{14}$: calcd: C 62.17, H 6.49, found: C 61.03, H 6.20.

4-{4'-[3,4,5-tri-(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoyloxy)]benzoyloxy}-benzoic acid (2_3^2)

Solid-phase synthesis:

After the preparation of the Wang resin, steps 1 and 2 of the general procedure were performed twice followed by steps 3 and 4. In step 4 1.2 eq (1.32 mmol, 859 mg) of the head group 3,4,5-tris(2-(2-(2-ethoxyethoxy)ethoxy)-ethoxy)benzoic acid are added. After cleavage from the resin, the crystallization from acetone afforded 840 mg (0.94 mmol, 86 %) of a colorless waxy solid (m.p. 90 °C).

Synthesis in solution:

Step 1 and 2: see synthesis of 2_1^3 ; Step 3: 899 mg (1.27 mmol) 4-[3,4,5-tris(2-(2-(2-ethoxyethoxy)ethoxy)ethoxybenzoyloxy)]benzoic acid and 591 mg (2.54 mmol) benzyl-4-hydroxybenzoate in 20 ml DCM, 311 mg (1.02 mmol) DPTS and 525 mg (2.54 mmol) DCC in 5.0 ml DCM; Yield: 69.0 mg (77.4 μmol , 7 %) colorless waxy solid.

Analytical data from the solid-phase synthesis:

¹H NMR (CDCl₃, 400MHz): δ [ppm] = 1.18-1.22 (m, 9H, CH₃), 3.49-3.55 (m, 6H, OCH₂, H-22), 3.57-3.75 (m, 24H, OCH₂), 3.81-3.84 (m, 2H, OCH₂, H-17_{para}), 3.86-3.90 (m, 4H, OCH₂, H-17_{meta}), 4.22-4.25 (m, 4H, OCH₂, H-16_{meta}), 4.27-4.29 (m, 2H, OCH₂, H-16_{para}), 7.33-7.38 (AA'BB', 4H, CH, H-4/4', H-9/9'), 8.17-8.21 (AA'BB', 2H, CH, H-8/8'), 8.26-8.30 (AA'BB', 2H, CH, H-3/3'); **¹³C NMR** (CDCl₃, 100 MHz): δ [ppm] = 15.15 (CH₃), 66.65 (OCH₂, C-22), 69.06 (OCH₂, C-16_{meta}), 69.64 (OCH₂, C-17_{meta}), 69.81, 69.83, 70.62, 70.70, 70.72, 70.87 (OCH₂), 70.60 (OCH₂, C-17_{para}), 72.56 (OCH₂, C-16_{para}), 109.87 (CH, C-13/13'), 121.89 (CH, C-9/9'), 122.21 (CH, C-4/4'), 123.51 (Cq, C-15), 126.59, 127.04 (Cq, C-5, C-10), 131.90 (CH, C-8/8'), 131.96 (CH, C-3/3'), 143.70 (Cq, C-14), 152.55 (Cq, C-12), 155.11 (Cq, C-7), 155.47 (Cq, C-2), 163.83 (C=O, C-1), 164.11 (C=O, C-11), 169.64 (C=O, C-6); **HRMS (ESI)**: m/z (%): calcd: 908.4280 ([M+NH₄]⁺, 100), found: 908.4278 ([M+NH₄]⁺, 100); **Elemental analysis** (%) for C₄₅H₆₂O₁₈: calcd: C 60.66, H 7.01, found: C 60.23, H 7.15.

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